

Application No.: 10/821,710

5

Docket No.: 546322000304

**REMARKS**

Reconsideration in light of the following remarks is respectfully requested. Applicants seek to amend independent claim 44 to put it and the dependent claims in condition for allowance or in better condition for appeal, cancel claims 49-55 and amend claims 56 and 57 to change their dependency in light of canceling claims 49-55. Therefore, this amendment after final is submitted in accordance with 37 C.F.R. §1.116. Claims 44, 47-48, and 56-63 will be pending.

**Amendment to the Specification**

In light of the Examiner's rejections in the pending Office Action, applicants respectfully request that the Examiner enter the proposed amendment to the specification. The amendment seeks to clarify the sizes of the nucleotide sequences of the invention. The amendment introduces no new matter. The size range of at least about 1 to 200 nucleotides is already in the present application at page 25, lines 14-15. Furthermore, the size range of 20-30 nucleotides may be found in U.S. Patent No. 6,573,099 at Col. 6, lines 25-30. The present application claims priority to U.S. Patent No. 6,573,099 and incorporates this patent by reference. MPEP 601.01(p) indicates that even "essential information" may be incorporated by reference to U.S. patents and patent applications, where the essential information may include information needed to describe the invention, enable the invention and support the best mode of the invention.

**Priority**

The Examiner has asserted that the species claims 49-57 are not disclosed in the specification.

Applicants respectfully disagree with the Examiner's assertions. However, in order to facilitate prosecution in this case applicants have canceled claims 49-55 and amended claims 56 and 57 to correct the dependencies. Applicants request that the Examiner recognize the priority of the pending claims.

sf-1964878

Application No.: 10/821,710

6

Docket No.: 546322000304

Information Disclosure Statement

The Examiner has stated that he cannot find a PTO/SB/17 form submitted with the Supplemental Information Disclosure Statement submitted on April 29, 2005. Applicants have included a copy of the post card returned by the OPIE. The post card clearly indicates that the PTO/SB/17 form was sent (See Item number 2 "Fee Transmittal") and given that the OPIE stamped and returned the form, the USPTO has received said form. Furthermore, the applicants were able to find the PTO/SB/17 form on Private PAIRS as the first page of a document titled, "Information Disclosure Statement (IDS) Filed" dated 4/29/05. A duplicate copy of the PTO/SB/17 form as filed April 29, 2005 has been provided for the Examiner's convenience.

Applicants respectfully request that the Examiner consider the references submitted with the Supplemental Information Disclosure Statement.

Oath/Declaration

The Examiner has objected to the oath or declaration stating that it is defective because the application is a continuation-in-part.

Applicants respectfully disagree. However, in order to facilitate prosecution in this case applicants have canceled claims 49-55 and amended claims 56 and 57 to correct the dependencies. Thus, the application cannot be considered a continuation-in-part as no alleged new matter remains in the application. Applicants request that the Examiner withdraw the objection to the oath or declaration.

Examiner has asserted that even with the removal of the subject matter objected to he would continue to consider the application a continuation-in-part; however, applicants are unaware of any support for this position in the MPEP. Section 2163.06 clearly indicates that an Examiner may both object to entry of an amendment as new subject matter and reject claims as lacking written description support but that the objection and rejection are to be withdrawn when the offending subject matter are removed. The application as filed was the same as application from which it was filed as a continuation. The claims with the allegedly offending subject matter were added by

sf-1964878

Application No.: 10/821,710

7

Docket No.: 546322000304

preliminary amendment. Sections 602.01 and 602.02 of the MPEP as cited by the Examiner do not appear to provide support for maintaining the objection to the oath or declaration. If the Examiner intends to maintain his objection to the applicants respectfully request that the Examiner cite to support in the MPEP for such position so that the applicants can understand the nature of such position.

#### Specification

The Examiner has objected to the specification as failing to provide antecedent basis for the claimed subject matter.

Applicants respectfully disagree. However, in order to facilitate prosecution in this case applicants have canceled claims 49-55 and amended claims 56 and 57 to correct the dependencies. Applicants request that the Examiner withdraw the objection to the specification.

#### Claim Rejection – 35 U.S.C. § 112

The Examiner has rejected claims 44 and 47-61 under 35 U.S.C. 112, first paragraph, as allegedly not enabling any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants respectfully disagree. Recent developments in this field have indicated that the length of dsRNA is not the likely factor that is determinative in induction of the interferon response and as such claims to greater than 30 nucleotides would be enabled. However, in order to facilitate prosecution in this case applicants have amended claim 44 to include the recitation "20 to 30." As noted by the Examiner, dsRNA in this size range do not induce the interferon response.

Regarding the Examiner's assertion that there is unpredictability in obtaining an RNAi response using an siRNA targeted to any given region of any given gene, the unpredictability in RNAi is far less than that found in many other biological systems. The applicants respectfully disagree with the Examiner's assertion and the rejection based upon this assertion. The Examiner has not established a *prima facie* case of lack of enablement. The Examiner in applying the *Wands*

sf-1964878

Application No.: 10/821,710

8

Docket No.: 546322000304

factors in the previous Office Action to the presently claimed invention set the utility of the invention that needs to be enabled as far higher than is appropriate. One significant utility of the present invention is as a research tool. The claim itself sets forth the utility as "post-transcriptionally repressing, delaying or otherwise reducing expression of the target gene." Section 2107.01(II) of the MPEP clearly indicates that an invention must be "wholly inoperative" to lack utility and that a small degree of utility is sufficient. Thus, as long as the invention as claimed achieves the claimed result to a small degree, in this case reducing expression of the target gene, it has utility and only need be enabled to that small degree. Clearly, the ability to reduce expression of target genes of interest to a even to a small degree has utility as a research tool to evaluate whether the expression of the target gene is tightly regulated or if small changes in expression do not affect the overall activity.

With this level of utility that needs to be enabled in mind, the invention has clearly been enabled. As noted by the Examiner, to be enabled, one of skill in the art must be able to make and use the claimed invention without undue experimentation. The relevant factors to be considered when evaluation whether undue experimentation is required are: (1) the state of the prior art; (2) the level of predictability of the prior art; (3) the amount of direction provided by the inventor; (4) the presence of working examples; (5) the skill in the art; (6) the amount of experimentation required; and (7) breadth of the claims. With regard to the state of the prior art and the level of predictability in the prior art, Dietz is not relevant to the present invention as antisense RNA works by a different mechanism. siRNA is much more effective, which is why siRNA is the method of choice today to reduce gene expression. Holen *et al.* (2002) *Nucl. Acids Res.* 30:1757-1766 strongly support the predictability of the presently claimed invention. While Holen *et al.* found a wide range of activities, most if not all of the constructs tested had some effect on the expression and thereby met the required level of utility to support enablement. McManus *et al.* (2002) *J. Immunol.* 169:5754-5760 also support the fact that the presently claimed invention is enabled. McManus *et al.* found that at its lowest one in five constructs provided full silencing (which as discussed is a much higher level of activity than is required to support enablement). In most biological systems, 20% success is quite high. For example, generating a transgenic animal by cloning is only successful from 1-5% of

sf-1964878

Application No.: 10/821,710

9

Docket No.: 546322000304

the time yet the USPTO routinely allows claims to transgenic animals. Thus, even in the worst case scenario of 20% success, this is clearly sufficient predictability. Further, McManus *et al.* note that more commonly the success rate is 50%, i.e., if one of skill in the art desires to create a construct that has the claimed function, they only need to generate two constructs and test for activity (and again the activity McManus *et al.* are referring to is much higher than the activity needed to support enablement). Thus, the predictability is much higher than is typical for biotech inventions that the USPTO routinely allows.

Regarding the amount of direction provided by the inventor and the existence of working examples, while the Examples in the specification are prophetic, they do in fact work as asserted in the specification. Furthermore, the Examples may be easily modified for use with other target genes by one of ordinary skill in the art without undue experimentation. Thus, the specification provides clear guidance that would allow one of skill in the art to perform the invention because the prophetic examples do in fact work.

Regarding the skill in the art and quantity of experimentation needed to make and use the invention, as noted by the Examiner, the skill in the art is high. As to the quantity of experimentation needed, as the Examiner has noted from McManus *et al.* typically only two constructs need to be tested to find a functional siRNA molecule that *silences* a gene (when all that is required for utility is to reduce the expression). Even in the worst case scenario, one of skill in the art need only test five constructs to find a functional siRNA molecule that silences a gene. Making five constructs is incredibly easy. As of the priority date of the application, one of skill in the art could order five siRNA molecules purified and ready to test from a company. Testing the five molecules only requires trivial molecular biology assays that were easily within the abilities of one of ordinary skill in the art. Thus, the amount of experimentation required is minimal and requires only the application of routine techniques that are well within the skill level of one of ordinary skill in the art.

sf-1964878

Application No.: 10/821,710

10

Docket No.: 546322000304

Thus, all of the factors strongly support the fact that one of skill in the art would not need to conduct undue experimentation to make and use the claimed invention. Thus, claimed invention is enabled. Therefore, the applicants respectfully request that the Examiner withdraw the rejection of claims 44 and 47-61.

Claim Rejection – 35 U.S.C. § 102(a)

The Examiner has rejected claims 44 and 47-61 as allegedly being anticipated by Harborth *et al.* *Antisense Nucl. Acid Drug Devel.* 13:83-105.

Applicants respectfully disagree. However, in order to facilitate prosecution in this case applicants have canceled claims 49-55 and amended claims 56 and 57 to correct the dependencies. The remaining pending claims are entitled to the earliest claim of priority for the present application which is March 20, 1998. Therefore, Harborth *et al.* fails to qualify as 102(a) prior art as it was published after the priority date of the present claims.

Furthermore, the Examiner's maintaining the rejection of claims 44 and 58-61 is improper as the Examiner has admitted that the limitations of the claims were described, but the Examiner asserted that the claims were not enabled as of the priority date and therefore not entitled to the priority date. Applicants have never encountered a 102 rejection based upon the assertion that the pending claims were not entitled to the priority date due to lack of enablement. Applicants are unaware of any support for this position in the MPEP. If the Examiner intends to maintain his objection to the applicants respectfully request that the Examiner cite to support in the MPEP for such position so that the applicants can understand the nature of such position. Even if there is support for such position, the applicants have rebutted the lack of enablement rejection as set forth above.

Applicants respectfully request that the Examiner withdraw the rejection of claims 44 and 47-61.

sf-1964878

Application No.: 10/821,710

11

Docket No.: 546322000304

The Examiner has rejected claims 44, 47, 54 and 56-61 as allegedly being anticipated by McManus *et al.* (2002) *RNA* 8:842-850.

Applicants respectfully disagree. However, in order to facilitate prosecution in this case applicants have canceled claims 49-55 and amended claims 56 and 57 to correct the dependencies. The remaining pending claims are entitled to the earliest claim of priority for the present application which is March 20, 1998. Therefore, McManus *et al.* fails to qualify as 102(a) prior art as it was published after the priority date of the present claims.

Furthermore, the Examiner's maintaining the rejection of claims 44 and 58-61 is improper as the Examiner has admitted that the limitations of the claims were described, but the Examiner asserted that the claims were not enabled as of the priority date and therefore not entitled to the priority date. Applicants have never encountered a 102 rejection based upon the assertion that the pending claims were not entitled to the priority date due to lack of enablement. Applicants are unaware of any support for this position in the MPEP. If the Examiner intends to maintain his objection to the applicants respectfully request that the Examiner cite to support in the MPEP for such position so that the applicants can understand the nature of such position. Even if there is support for such position, the applicants have rebutted the lack of enablement rejection as set forth above.

Applicants respectfully request that the Examiner withdraw the rejection of claims 44, 47, 54 and 56-61.

The Examiner has rejected claims 44, 47, 49-53, 56, 57, 60 and 61 as allegedly being anticipated by Elbashir *et al.* (2002) *Methods* 26:199-213.

Applicants respectfully disagree. However, in order to facilitate prosecution in this case applicants have canceled claims 49-55 and amended claims 56 and 57 to correct the dependencies. The remaining pending claims are entitled to the earliest claim of priority for the present application which is March 20, 1998. Therefore, Elbashir *et al.* fails to qualify as 102(a) prior art as it was published after the priority date of the present claims.

sf-1964878

Application No.: 10/821,710

12

Docket No.: 546322000304

Furthermore, the Examiner's maintaining the rejection of claims 44 and 58-61 is improper as the Examiner has admitted that the limitations of the claims were described, but the Examiner asserted that the claims were not enabled as of the priority date and therefore not entitled to the priority date. Applicants have never encountered a 102 rejection based upon the assertion that the pending claims were not entitled to the priority date due to lack of enablement. Applicants are unaware of any support for this position in the MPEP. If the Examiner intends to maintain his objection to the applicants respectfully request that the Examiner cite to support in the MPEP for such position so that the applicants can understand the nature of such position. Even if there is support for such position, the applicants have rebutted the lack of enablement rejection as set forth above.

Applicants respectfully request that the Examiner withdraw the rejection of claims 44, 44, 47, 49-53, 56, 57, 60 and 61.

Claim Rejection – 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 44 and 47, 48, and 58-61 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention..

Applicants respectfully disagree. However, in order to facilitate prosecution in this case applicants have amended claim 44 to replace the recitation "greater than 20-100" with "20 to 30." Applicants therefore request that the Examiner withdraw the rejection of claim 44, 47, 48 and 58-61.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

sf-1964878



Application No.: 10/821,710

13

Docket No.: 546322000304

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 546322000304. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: August 25, 2005

Respectfully submitted,

By   
Otis Littlefield

Registration No.: 48,751  
MORRISON & FOERSTER LLP  
425 Market Street  
San Francisco, California 94105-2482  
(415) 268-6846

sf-1964878